Extent of resection of peritumoral diffusion tensor imaging-detected abnormality as a predictor of survival in adult glioblastoma patients

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Resection of more peritumoral DTI abnormalities correlate with improved survival in glioblastoma patients

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Extent of DTI resection in glioblastoma

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ABSTRACT

OBJECTIVE Diffusion tensor imaging (DTI) has been shown to detect tumor invasion in glioblastoma patients and has been applied in surgical planning. However, the clinical value of the extent of resection based on DTI is unclear. Therefore, the correlation between the extent of resection of DTI abnormalities and patients' outcome was retrospectively reviewed.

METHODS A review was conducted of 31 patients with newly diagnosed supratentorial glioblastoma who underwent standard 5-aminolevulinic acid-aided surgery with the aim of maximal resection of the enhancing tumor component. All patients underwent presurgical MRI, including volumetric postcontrast T1-weighted imaging, DTI, and FLAIR. Postsurgical anatomical MR images were obtained within 72 hours of resection. The diffusion tensor was split into an isotropic (p) and anisotropic (q) component. The extent of resection was measured for the abnormal area on the p, q, FLAIR, and postcontrast T1-weighted images. Data were analyzed in relation to patients' outcome using univariate and multivariate Cox regression models controlling for possible confounding factors including age, O6-methylguanine-DNA-methyltrans-ferase methylation status, and isocitrate dehydrogenase-1 mutation.

RESULTS Complete resection of the enhanced tumor shown on the postcontrast T1-weighted images was achieved in 24 of 31 patients (77%). The mean extent of resection of the abnormal p, q, and FLAIR areas was 57%, 83%, and 59%, respectively. Increased resection of the abnormal p and q areas correlated positively with progression-free survival ($p = 0.009$ and $p = 0.006$, respectively). Additionally, a larger, residual, abnormal q volume predicted significantly shorter time to progression ($p = 0.008$). More extensive resection of the abnormal q and contrast-enhanced area improved overall survival ($p = 0.041$ and 0.050, respectively).

CONCLUSIONS Longer progression-free survival and overall survival were seen in glioblastoma patients in whom more DTI-documented abnormality was resected, which was previously shown to represent infiltrative tumor. This highlights the potential usefulness and the importance of an extended resection based on DTI-derived maps.

Key words: glioblastoma, extent of resection, diffusion tensor imaging, volumetric study, progression free survival

ABBREVIATIONS

5-Ala = 5-aminolevulinic acid; DT = diffusion tensor; DTI = diffusion tensor imaging; EOR = extent of resection; FLAIR = fluid-attenuated inversion recovery; FLIRT = FMRIB Linear Image Registration Tool; FMRIB = Oxford Centre for Functional MRI of the Brain; FOV = field of view; FSL = FMRIB Software Library; IDH-1 = isocitrate dehydrogenase-1; HR = hazard ratio; MGMT = O6-methylguanin-DNA-methyltransferase; p = isotropic component; q = anisotropic component.

INTRODUCTION

Glioblastoma is the most prevalent malignant primary brain tumor and one of the leading cancers in terms of years of life lost.[15] Standard treatment for this highly malignant disease includes maximal safe resection followed by concomitant chemoradiotherapy and adjuvant chemotherapy with temozolomide. However, the prognosis remains poor, with 2- and 5-year survival rates of only 27% and 9.8%, respectively.[27]

The main factors influencing prognosis are age, performance status, tumor molecular type, and extent of resection (EOR), of which the former three are fixed and the latter can be changed. Therefore, many efforts have made to improve the extent of maximal tumor resection while preserving normal brain tissue and function. Resection of a larger fraction of the tumor results in a longer life expectancy.[6,7,12] To achieve maximal tumor resection, intraoperative neuronavigation, 5-aminolevulinic acid (5-ALA) and other imaging techniques (e.g., intraoperative MRI or ultrasound) have been introduced. Use of 5-ALA increased the EOR to 65% of the total contrast-enhanced area and prolong the progression-free survival.[24] A contrast-enhanced T1-weighted signal has many limitations in accuracy of the delineation of tumor margin.[19] Consequently, the clinical benefit of resection outside the contrast-enhanced area has been investigated.[13] Recently, it has been shown that extending the resection to the peritumoral high T2 signal areas beyond the enhanced lesion on postcontrast T1-weighted images can provide longer survival than less extensive resections.[13] This is thought to be due to tumor infiltration beyond the contrast-enhanced area.[20] However, a high signal on T2-weighted imaging is not specific for tumor infiltration, because it is also caused by edema.

Diffusion tensor imaging (DTI) is able to detect tumor extent beyond the contrast-enhanced area because of subtle white matter changes.[17] By decomposing the diffusion tensor into an isotropic component (p) and an anisotropic component (q),[16] white matter that is infiltrated or disrupted by the glioblastoma can be identified.[17] Radiotherapy treatment plans based on

peritumoral abnormal DTI areas were able to achieve a large reduction of 15%–35% in planning target dose and 50% of clinical target volume, which minimized radiation complication without affecting the survival.[1,8] In addition, DTI changes, especially those determined by p mapping, can be used to evaluate early treatment response after temozolomide chemotherapy in glioma patients.[2] However, to our knowledge, there are no studies to date showing a clinical benefit of resecting the abnormal peritumoral DTI area. This prompted our study analyzing the influences of the EOR of abnormal peritumoral DTI areas on patients' outcome.

METHODS

Patient Population

We included 31 glioblastoma patients (mean age 56 years, range 31–68 years; 19 men and 12 women) from our consecutive cohort. All patients had a Karnofsky Performance Scale score of 70 or higher and had presurgical MR scans with follow-up MRI available after tumor resection. Patients were deemed suitable for undergoing complete resection of the contrast-enhancing tumor by 1 neurosurgeon (S.J.P.), and, with the goal of achieving maximum tumor resection, tumor resection was performed using neuronavigation (StealthStation; Medtronic) and 5-ALA fluorescence guidance. The presurgical images were acquired, on average, 1 day (range 0–9 days) before surgery. Follow-up MR scans were obtained as soon as possible after surgery and no later than 72 hours after surgery. Exclusion criteria were previous cranial surgery, previous cerebral radiotherapy, or a known other primary tumor.

All patients received standard concomitant and adjuvant temozolomide chemoradiotherapy[27] about 1 month after resection. O6-methylguanin-DNA-methyltransferase (MGMT) methylation was determined by pyrosequencing of the DMR2 region. Isocitrate dehydrogenase (IDH-1) R132H mutation status was analyzed using immunohistochemistry. Survival data were extracted from the medical records. Tumor eloquence was classified as

previously described.[12,22] The study was approved by the local institutional review board, and informed written consent was obtained from all patients.

MR data acquisition

Presurgical imaging was performed using a 3.0-T MR Magnetom system (Siemens Healthcare) with a standard 12-channel head coil. Imaging included T1-weighted imaging after contrast, T2-weighted FLAIR sequence, and DTI. A 3D T1-weighted scan with fat suppression was acquired after the intravenous injection of 9 ml of gadolinium (Gadovist; Bayer Schering Pharma) (TR/TE/TI 2300/2.98/900 msec; flip angle 9°; FOV 256 × 240 mm; 176–192 slices; no slice gap; and voxel size 1 × 1 × 1 mm). A 2D FLAIR sequence was obtained (TR/TE/TI 7840–8420/95/2500 msec; flip angle 150°; FOV 250 × 200 mm; 25–27 slices; 1-mm slice gap; and voxel size 0.78125 × 0.78125 × 4 mm). DTI data were acquired using a single-shot echo-planar sequence (TR/TE 8300/98 msec; flip angle 90°; FOV 192 × 192 mm; 63 slices; no slice gap; and voxel size 2 × 2 × 2 mm) with multiple b-values (0, 350, 650, 1000, 1300, and 1600 sec/mm2) scanned in 13 directions.

Direct postsurgical images were acquired on a 1.5-T Optima, a 1.5- or 3.0-T Signa, or a 3.0-T Discovery MR scanner (GE Healthcare) with standard head coil. Imaging included a T1-weighted anatomical sequence after the intravenous injection of 9 ml of gadolinium. This was performed as a 2D T1-weighted sequence (TR/TE 460–700/11–21 msec, flip angle 90°; FOV 220–260 × 220–260 mm; 20–85 slices; 0- to 1-mm slice gap; voxel size 0.429–0.5079 × 0.429–0.5079 × 2–6 mm) or a 2D T1 inversion recovery sequence (TR/TE/TI 2508–2600/12–42/780–920 msec; flip angle 90–110°; FOV 220 × 220 mm; 20–22 slices; 1- to 3.5-mm slice gap; and voxel size 0.4297 × 0.4297 × 6 mm).

Image processing

DT images were processed using tools from the Oxford Centre for Functional MRI of the Brain (FMRIB) Software Library (FSL) version 5.0.0 (fsl.fmrib.ox.ac.uk/fsl/fslwiki). DT images

were realigned to the b0-image to compensate for eddy currents and motion.[10] We calculated the isotropic component (p) and anisotropic component (q) after eigenvalues were calculated on multiple fiber directions at each voxel in the DTI data, as previously described.[16] For each subject, presurgical DT and FLAIR images were coregistered with presurgical postcontrast T1-weighted images by a linear transformation, using the default FMRIB linear image registration tool (FLIRT) functions provided by FSL.[10]

Coregistration between postsurgical and presurgical images was done by a semiautomatic coregistration methods. All images were fit into presurgical, volumetric contrast-enhanced T1-weighted images. First, we used automatic brain-extracted images,[9] which were manually corrected. Then we calculated the transformation between presurgical tumor and postsurgical resection cavity by using the linear FLIRT coregistration of the lesion, ventricle, and the external mask of the brain between presurgical and postsurgical images. This transformation was then used as input transformation matrix for an FMRIB nonlinear image registration tool to coregister the brain.

Tumor Volume and EOR Data analysis

Extent of resection was determined from the resection cavity in the coregistered, postsurgical, postcontrast T1-weighted image (Fig. 1, blue outline) by one of the authors (J.L.Y.) blinded to the outcome, with the agreement of a second author (A.H.). The 3D, peritumoral, abnormal FLAIR, p, and q regions of interest were manually selected on the coregistered presurgical MR images (Fig. 1B–1D). The interobserver correlation was done by the first author (J.L.Y.) and senior author (S.J.P.) with fair agreement. The coregistered resected region was extracted from the total abnormal presurgical region for each sequence, using Matlab (MathWorks Inc.). The resected volumes were calculated for the p, q, and FLAIR regions by multiplying all voxels of interests with the slice thickness in Matlab.

Statistical Analysis

Data were analyzed using SPSS version 22 (IBM Inc.). A Cox regression model was used to estimate the influence of the EOR based on p, q, FLAIR, and postcontrast T1-weighted images on progression-free survival and overall survival. Multivariate analysis included the following covariates: age, MGMT methylation status, IDH-1 mutation status, presurgical tumor volume based on postcontrast T1-weighted images, tumor location based on eloquence, and midline shift. These covariates were tested individually with the resection ratio of p, q, FLAIR, enhancing area on postcontrast T1-weighted image, and residual tumor volume based on different MR images. Subgroup analysis was done for a group with low and high abnormal q resection ratios by categorizing the patient based on the median of the whole group. Comparison of characteristics of patients in different groups was performed by using a t-test for continuous data because they showed a normal distribution tested by D'Agostino-Pearson normality test and the chi-square for dichotomous data. The chi-square test with Yates's correction was used for small-number contingency categorical analysis. A two-sided p value of 0.05 was used throughout. Mean results are presented ± SD.

RESULTS

Patients' Characteristics

Patients' clinical characteristics are shown in Table 1. Complete resection based on postcontrast T1-weighted imaging was achieved in 24 patients (77% of 31 patients). Ten patients had the tumor located within an eloquent area, which included the primary motor or sensory cortex, speech center, internal capsule, and basal ganglia. Ten patients had tumor located in a near-eloquent area, which included the supplementary motor area, corpus callosum, and proximity to the calcarine fissure and the speech center. The mean midline shift was 3.3 mm (± 3.7 mm; range 0–11.9 mm). The mean presurgical, contrast-enhanced tumor volume was 46 ml (± 30 ml; range 8–119 ml). The volume of the resection area was 53 ml (± 31 ml; range 10–131 ml), which was significantly larger than the presurgical tumor ($p = 0.001$). A total of 57% of the abnormal p area, 83% of the abnormal q area, and 59% of the

increased FLAIR signal area was resected. Residual tumor volume based on p, q, FLAIR, and postcontrast T1-weighted images was 38.4 ml (± 30.2 ml; range 4.4–129.4 ml), 8 ml (± 9.7 ml; range 0–36 ml), 40.7 ml (± 32.7 ml; range 0.4–127.9 ml), and 2.7 ml (± 6.8 ml; range 0–26.6 ml), respectively. None of the patients had a major postsurgical neurological deficit or Karnofsky Performance Scale score of less than 70, which was our condition to undergo temozolomide chemoradiotherapy.

Extent of Resection and Patients' Outcome

Univariate Cox regression models for each variable showed a significant correlation of progression-free survival with the EOR of the p area ($p = 0.030$), complete resection of the contrast-enhanced lesion ($p = 0.004$), and MGMT methylation status ($p = 0.041$). Multivariate analysis was used to test the EOR with other covariates (Table 2). The results showed that resection of the more abnormal p was a protective predictor of tumor progression (HR 0.911; $p = 0.009$). The EOR of abnormal q areas was also significantly correlated with progression-free survival in the multivariate analysis (HR 0.935; $p = 0.006$). The EOR based on FLAIR showed no association with progression-free survival in either univariate or multivariate analysis ($p = 0.994$ and $p = 0.799$, respectively). The presence of MGMT methylation was found to be a significant predictor of progression-free survival in the multivariate models for p (HR 4.626; $p = 0.009$), q (HR 6.716; $p = 0.006$), and FLAIR (HR 95.941; $p = 0.001$).

For overall survival, multivariate analysis was performed after controlling for age, MGMT methylation status, IDH-1 mutation status, presurgical tumor volume, tumor eloquence, and midline shift. Both the EOR based on the q map and the EOR based on postcontrast T1-weighted images were identified as predictors for overall survival (HR 0.965, $p = 0.041$; HR 9.946, $p = 0.050$, respectively). The MGMT methylation status was significantly associated with overall survival in the multivariate models for p map (HR 3.737; $p = 0.043$), q map (HR 4.932; $p = 0.012$), and FLAIR (HR 10.274; $p = 0.009$) images. Presurgical tumor volume based on postcontrast T1-weighted images was found to be a covariate associated with

increased hazard ratio relative to EOR of the q abnormality (HR 1.039; p = 0.024) and on the enhanced area of the postcontrast T1-weighted image (HR 1.037; p = 0.040).

Previous results indicated the importance of the EOR, especially q abnormality, on outcome; therefore, we explored this in more detail. Classifying patients into 2 groups by using the median of the extent of abnormal q resection resulted in a resection cutoff of 89% of the q abnormality. Patients with a resection of greater than 89% of the q abnormality had a significantly longer progression-free survival (mean 421 ± 311 days) than those with a resection of less than 89% of the abnormality (257 ± 214 days; p = 0.034) and better overall survival (621.9 ± 389.0 days vs 518.13 ± 264.7 days; p = 0.011) (Fig. 2). There was no statistical difference between these 2 subgroups in age, sex, tumor location, number of patients receiving a gross-total resection, or MGMT methylation or IDH-1 mutation status (Table 3). Similar results were seen when subgrouping patients with the median extent of p resection: Longer progression-free survival was shown in patients with greater than 60% resection of the p abnormal area (421 ± 311 vs 258 ± 176; p = 0.046).

In our study, 26 patients (83.9%) had tumor recurrence within 2 cm adjacent to the resection cavity. Three patients (9.7%) had distal recurrence more than 2 cm from the original resection cavity, and 2 had recurrence both locally and distally. All patients with solely distal recurrence received complete resection of the enhanced lesion shown on the postcontrast T1-weighted image and a greater EOR of the q abnormal area (97.7%) than the others (87.4%), and 2 were MGMT methylated. Progression-free survival (721 ± 270 days) and overall survival (954 ± 461 days) were also longer in patients with distal recurrence.

Residual Tumor Volume and Patient Outcome

The correlations of patients' outcome and residual tumor volume based on different MR images are summarized in Table 4. A larger residual volume on DTI was associated with a decrease in progression-free survival, which was statistically significant for the q abnormality

(HR 1.118; p = 0.008), while residual volume of the p abnormality was not significant (HR 1.28; p = 0.074). Residual FLAIR volume was not correlated with progression-free survival. Overall survival was not influenced by the residual abnormal p, q, or contrast-enhanced lesion volumes. Residual FLAIR volume decreased the hazard ratio of overall survival (HR 0.942; p = 0.008).

DISCUSSION

In this study, we retrospectively reviewed the correlation between the EOR based on DTI and patients' outcome. Although the intention of initial resection was based on 5-ALA rather than on any DTI parameter, this study showed, via multivariate Cox regression model, a significant correlation between the EOR, based on both the p map and q map, and progression-free survival. Furthermore, a favorable overall survival was seen in patients who received greater resection of the q map and the enhanced area on postcontrast T1-weighted images. Thus, by resecting more abnormal DTI areas, most importantly the q area, the infiltrating tumor burden decreases, leading to a better outcome.

The significance of resecting more of a contrast-enhanced lesion has been shown clearly to correlate with patient survival. Sanai and colleagues showed that improved overall survival begins at a 78% resection and continues to increase as resection of the contrast-enhanced area becomes greater.[21] A nonvolumetric study of high-grade glioma has also shown a longer overall survival associated with complete resection rather than with incomplete resection (16.7 vs 11.8 months, respectively; p < 0.001).[25] Others have reported the synergic clinical benefit of the EOR and concomitant chemoradiotherapy.[23] Moreover, the benefit of reduced tumor burden is related to the efficacy of 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU): In one study, a lower concentration was needed to achieve 90% growth inhibition in low-tumor-burden groups.[14] In patients receiving BCNU wafers during surgery, longer median survival has been noted in the complete-resection group compared with those in the subtotal-

resection group.[26] Therefore, reduction of contrast-enhancing tumor burden is an important prognostic factor for patient outcome.

To date, most studies have defined EOR using the contrast-enhanced area only; however, a false-negative rate of 16% was found in normal-appearing areas on T1-weighted images,[17] and tumor cells often extend beyond the contrast-enhanced area. We have shown previously that specific DTI signatures can predict this microscopic tumor invasion.[17,18] In particular, regions with greater than a 10% increase of p signified white matter infiltration by tumor, whereas regions with greater than a 12% decrease in q showed white matter disruption by cancer. Therefore, using DTI can better delineate the actual tumor margin and show the invasive area of tumor. Although we did not perform a histological correlation in this study, previous research has validated a correlation between DTI and viable tumor cells.[4]

A previously conducted tumor-resection treatment-bias study showed that complete resection was more often achieved in younger patients and in those with tumors in noneloquent tumor locations.[25] We tested our result by using a median q-abnormality EOR of 89% as the cutoff to stratify patients into 2 groups. In these groups, a longer progression-free survival was seen in those with a greater than 89% q-abnormality resection, but other variables, including age, tumor eloquence, MGMT methylation status, IDH mutation, midline shift, presurgical tumor size, and complete resection of the enhanced lesion on postcontrast T1-weighted images, were all comparable (Table 3). A bias, therefore, could not be identified, which strengthens our results, indicating the importance of the EOR based on DTI.

Specifically looking at the patients with distal recurrence, a previous study showed a correlation between extended resection and recurrence pattern, with a better prognosis in those with distal recurrence.[3] In our study, all 3 patients with distal recurrence received a greater EOR of the DTI-detected abnormality (EOR of q abnormality > 97%) beyond the contrast-enhanced area. Although the number in our study is small, this finding may indicate

that distal recurrence occurs in those with a better local control based on DTI and consequently resulted in a better prognosis.

We also examined the residual tumor volume based on different MR sequences. More abnormal q volume left after surgery can significantly increase the risk of progression and marginally decrease overall survival. Grabowski and colleagues showed that residual contrast-enhanced lesion volume of more than 2 cm3 after surgical resection was a strong, unfavorable predictor of overall survival.[5] Furthermore, others also concluded that a residual contrast-enhanced tumor volume of less than 10 cm3 can lead to both prolonged time to progression and survival.[11] In our results, only marginal significance in progression-free survival was noted based on postcontrast T1-weighted imaging. This may be due to the limited numbers of patients in our study. Regardless of the limited numbers, we clearly displayed the advantage of the q map, which, according to a previous biopsy studies, represents regions of tumor cells.[17] Thus, a smaller residual abnormality in the q region indicated a lower tumor load and a better prognosis.

CONCLUSION

The expanding application of DTI in patients with brain tumors can demonstrate not only possible tumor invasion but also can provide a guide for surgeons. Our results underscore the importance of abnormal DTI area, especially of abnormal q area, showing that patients who received larger EOR and who had less residual abnormal DTI had better progression-free survival and overall survival. Further prospective studies are needed to clarify the clinical benefit of incorporating DTI into surgical planning.

DISCLOSURE

None of the authors have financial of other conflict of interest related to the work presented in this paper.

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TABLE 1 - Patient Characteristics

Total number of patients	31
Male	19
Female	12
Age (years)	56 ± 11
Tumor location	
Eloquent	10
Near eloquent	12
Non eloquent	9
Midline shift (mm)	3.3 ± 3.7
Presurgical tumor size (mL)	
T1 contras enhanced	46 ± 30
FLAIR	84 ± 44
Isotropic (p) DTI	83 ± 44
Anisotropic (q) DTI	51 ± 23
EOR, by image type, %	
T1 post contrast	136 ± 71
FLAIR	58 ± 21
Isotropic (p) DTI	57 ± 18
Anisotropic (q) DTI	83 ± 20
Residual tumor size, by image type, (mL)	
T1 post contrast	2.7 ± 6.7
FLAIR	41 ± 32
Isotropic (p) DTI	38 ± 30
Anisotropic (q) DTI	8 ± 9.6
GTR (based on contrast) no. of patients	24
STR (based on contrast) no. of patients	7
IDH-1 positive	3
MGMT methylation positive	10
Progression free survival (days)	367 ± 263
Overall survival (days)	559 ± 292

GTR = gross-total resection; STR = subtotal resection; T1C = postcontrast T1-weighted image. Data are given as mean ± SD unless otherwise indicated.

TABLE 2 - Extent of Resection and Patients' Outcome

	Progression Free Survival			Overall Survival		
	p-value	HR	CI (95%)	*p*-value	HR	CI (95%)
p	0.009†	0.911	0.850-0.977	0.795	0.993	0.940-1.049
q	0.006†	0.935	0.891-0.980	0.041†	0.965	0.934-0.999
FLAIR	0.799	0.997	0.926-1.061	0.052	1.062	1.999-1.129
T1C resection	0.094	6.499	0.727-58.069	0.050†	9.946	1.005-98.464

Multivariate analysis results showing age, MGMT methylation status, IDH-1 mutation status, presurgical tumor volume based on postcontrast T1-weighted, midline shift, and tumor eloquent location as covariates. †Statistically significant.

TABLE 3 - Patient characteristics for the subgroups of p resection area

	p EOR < 60%	p EOR > 60%	*p*-value
Male	9	10	1
Female	6	6	
Age, yrs	53.67 ± 13.16	58.68 ± 8.8	0.4168
Tumor location, no.			0.1298
Eloquent	5	5	
Near eloquent	8	4	
Noneloquent	2	7	
Midline shift, mm	3.33 ± 3.90	3.65 ± 3.63	0.8138
Presurgical tumor size, by imaging type, ml			
T1C	35.9 ± 18.4	53.3 ± 30.6	0.0682
FLAIR	81.1 ± 37.8	95.8 ± 52.2	0.3888
Isotropic (p) DTI	80.1 ± 38.1	90.9 ± 48.2	0.4948
Anisotropic (q) DTI	48.8 ± 14.3	54.5 ± 30.8	0.5147
GTR,‡ no. of patients	9	15	0.0693
STR,‡ no. of patients	6	1	
IDH-1 positive, no. of patients	2	1	0.5050
MGMT methylation positive, no. of patients	5	5	0.9013
Progression-free survival‡, days	257 ± 214	421 ± 311	0.034†
Overall survival,§ days	518.13 ± 264.7	621.9 ± 389.0	0.011†

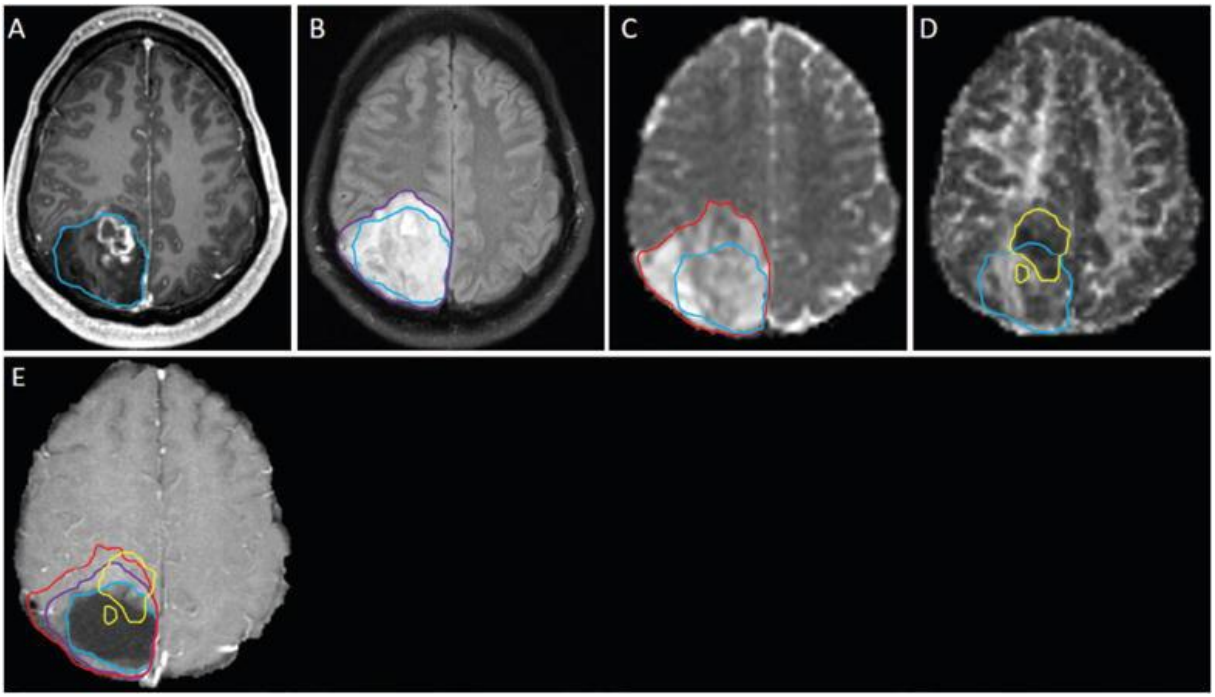
Data given as mean ± SD unless otherwise indicated. †Statistically significant. ‡Based on contrast. §Analyzed using multivariate Cox regression model..

Table 4 - Residual Tumor Volume and Patients' Outcome

	Progression Free Survival				Overall Survival			
	p-value	HR	CI (95%)		*p*-value	HR	CI (95%)	
T1C	0.060	1.393	0.986–1.969	0.401	1.140	0.840–1.549	T1C	
Isotropic (p) DTI	0.074	1.028	0.997–1.059	0.942	0.999	0.970–1.029	Isotropic (p) DTI	
Anisotropic (q) DTI	0.008†	1.118	1.029–1.215	0.080	1.053	0.994–1.116	Anisotropic (q) DTI	
FLAIR	0.882	1.003	0.968–1.038	0.008	0.939	0.897–0.983	FLAIR	

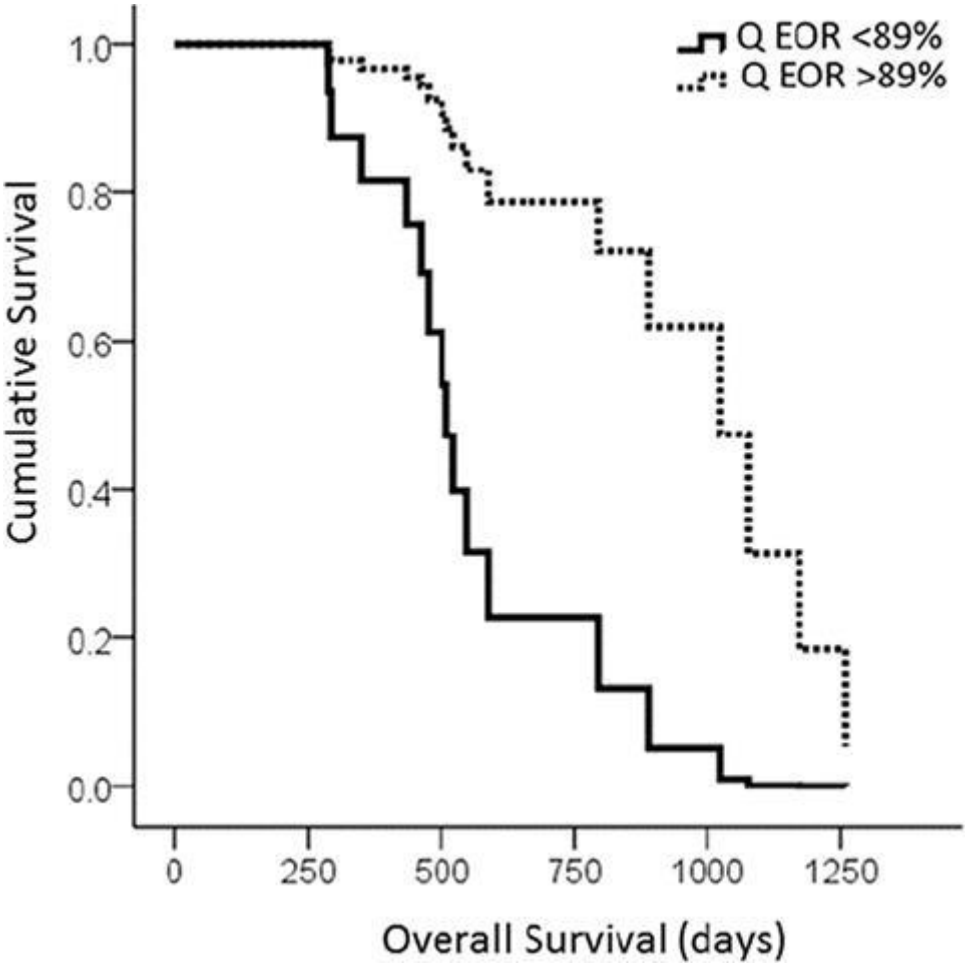
Multivariate analysis results showing age, MGMT methylation status, IDH-1 mutation status, presurgical tumor volume based on T1 contrast imaging, midline shift, and tumor eloquent location as covariates. †Statistically significant.

FIGURE 1 - Regions of interest and EOR



Presurgical postcontrast T1-weighted image (A), FLAIR (B), and diffusion tensor images (C and D) are shown with the resected area contoured in blue in a representative patient. The abnormal FLAIR region (B, purple), the isotropic abnormality (C, red) and the anisotropic abnormality (C, yellow) are outlined. E: Summary of the regions of interest in a postsurgical contrast-enhanced T1-weighted image.

FIGURE 2 – Patient overall survival according to abnormal q resection ratio



Cox regression survival analysis showed that patients with a resection of greater than 89% of the q abnormality had a better overall survival than patients with less than 89% resection ($p = 0.011$).